PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference SCB/61737001	**FOR FURTHER ACTION** See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB 03/04725	International filing date *(day/month/year)* 03.11.2003	Priority date *(day/month/year)* 04.11.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/352		
Applicant GW PHARMA LIMITED		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand 03.06.2004	Date of completion of this report 23.02.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Veronese, A Telephone No. +49 89 2399-7824

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/04725

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-8 as originally filed

Claims, Numbers

1-20 as originally filed

Drawings, Sheets

1/3-3/3 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees, the applicant has:

☐ restricted the claims.

☒ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☒ all parts.

☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	10, 16, 18,20
	No:	Claims	1, 2, 3, 4, 5 ,6, 7, 9, 11, 12, 13, 14, 15, 17, 19 No
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-20 (No)
Industrial applicability (IA)	Yes:	Claims	
	No:	Claims	1-20 (yes)

2. Citations and explanations

see separate sheet

SECTION IV
Lack of unity of invention

This IPEA agrees with the objection as to lack of unity put forward by the ISA, for the reasons already given in Form PCT/ISA/206. Since the Applicant, upon invitation, has paid an additional search fee and an additional examination fee, the present Opinion will be drawn in respect of both the two inventions identified in Form PCT/ISA/206.
These two inventions relate to:
1) the use of cannabinoids in relation to the treatment of neuropathic and chronic pain
2) the use of cannabinoids in relation to the treatment of seep disturbance

INVENTION N.1

SECTION V
Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents; unless otherwise indicated, reference is made to the relevant passages emphasized in the Search Report.
D1 (WO02064109)
D2 (WO02069993)

NOVELTY (Art.33(3) PCT)

D1 (WO02064109, page 27, line 5-15, 27-33; page 28, line 15-17; page 28, line 34 - page 29, line 2; page 31, line 3-10; page 33, line 5-15; claims 26, 29, 45, 49, 53, 78) discloses compositions comprising cannabinoids (preferred are mixture of tetrahydrocannabinol (THC) and cannabidiol (CBD)). These compositions are used for the treatment of neuropathic and chronic pain (cancer pain). Compositions comprising a 1:1 mixture of THC and CBD are preferred for the treatment of neuropathic pain (see table 4). These compositions can be in the form of plant extracts and can be administered in the form of a sublingual or buccal spray.
In view of this prior art, the subject matter of claims 1, 2, 3, 4, 5 ,6, 9 is not new in the sense of Art.33(2) PCT.
D2 (WO02069993, page 1, line 5-10, 29-31; page 2, line 10-21; page 3, line 12-15; page 7, line 38 - page 8, line 1; page 8, line 22-33; examples 1, 2 and claims) discloses pharmaceutical compositions comprising tetrahydrocannabinol (THC) and cannabidiol (CBD) in ratio 3:1-1:2; and preferably in ratio 2:1. These compositions are used for the

treatment of chronic pain, of cancer pain and of pain occurring in multiple sclerosis. Plant extracts comprising the cannabinoids are also disclosed. Dosage forms for delivering less than 37.5 mg THC are disclosed.
In view of this prior art, the subject matter of claims 1, 2, 3, 4, 5 , 7, 9 is not new in the sense of Art.33(2) PCT.

INVENTIVE STEP (Art.33(3) PCT)

Most of the subject matter related to the first invention appears to be anticipated by D1 and D2. The subject matter which is still new (for example the selection of certain specific dosages or dosage ratios between the cannabinoids, or the treatment of certain specific forms of pain) does not seem to be characterized by any new technical feature providing surprising or unexpected technical effect over the prior art. For this reason the subject matter of claims 8, 10 does not seem to involve an inventive step in the sense of Art.33(3) PCT.
Note: since the priority of the present application appears to be valid, the intermediate document GB2377633 is not considered as prior art for establishing novelty and inventive step of the present application.

INDUSTRIAL APPLICATION

The subject matter of claims 1-10 is industrially applicable.

INVENTION N.2

SECTION V
Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents; unless otherwise indicated, reference is made to the relevant passages emphasized in the Search Report.

D2: WO 02/069993 A (WERNER MICHAE et al.) 12 September 2002
D3: WO 02/080903 A (RADULOVACKI MIODRAG et al.) 17 October 2002
D4: WO 02/056932 A (EMLIN BIOSCIENCES) 25 July 2002 (2002-07-25)
D5: DATABASE MEDLINE [Online] US NATIONAL LIBRARY OF MEDICINE (NLM), BETHESDA, MD, US; August 1981 (1981-08) CARLINI E A ET AL: 'Hypnotic and antiepileptic effects of cannabidiol.' Database accession no. NLM7028792 XP002277010 & JOURNAL OF CLINICAL PHARMACOLOGY. US 1981 AUG-SEP, vol. 21, no. 8-9 Suppl, August 1981, pages 417S-427S.

NOVELTY (Art.33(2) PCT)

D2 (WO02069993, page 1, line 5-10, 29-31; page 2, line 10-21; page 9, line 5, 6, 7; claims 1,2,3,4, 7,8,10); examples 1, 2) discloses pharmaceutical compositions comprising tetrahydrocannabinol (THC) and cannabidiol (CBD) in ratio 3:1-1:2; and preferably in ratio 2:1. The use of these compositions for the treatment of sleep disorders (insomnia) is also disclosed (see page 9, line 5,6,7). Plant extracts comprising the cannabinoids are also disclosed. Dosage forms for delivering less than 37.5 mg and less then 10 mg THC are also disclosed.
In view of this prior art, the subject matter of claims 11, 12, 13, 14, 15, 17, 19 is not new in the sense of Art.33(2) PCT.
D3 (WO 02/080903, see page 7, lines 7-19 , 25; figures 1a, 1b, 2a, 4; claims 1,5) discloses the administration of a cannabinoids (THC, 9-tetrahydrocannabinol cannabidiol being among the preferred ones), for the treatment of a sleeping disorder (a sleep related breathing disorder).
D4 (WO 02/056932, see page 4, lines 4-11, 15; claims 1, 9, 22, 23) discloses delivery devices for the administration of drugs (cannabinoids are the preferred drugs) for treatment of a number of diseases. Sleep disorders are also mentioned.
D5 (XP002277010, see abstract) discloses the hypnotic effect of cannabidiol.
In view of D3, D4, D5 the subject matter of claims 11,12 is not new.

INVENTIVE STEP (Art.33(2) PCT)

Most of the subject matter relating to the second invention claimed in the present application is anticipated by D2-D5. The subject matter which is still new (for example the selection of certain specific dosages or dosage ratios between the cannabinoids, or of certain specific forms of pain) does not seem to be characterized by any new technical feature providing any surprising or unexpected technical effect over the prior art. Also, from the data reported in the figures it appears that the administration of 1:1 ratios of THC and CBD does not provide significant differences as compared to the administration of THC alone.
For this reason the subject matter of claims 16, 18, 20 does not seem to involve an inventive step over the prior art.

INDUSTRIAL APPLICATION

The subject matter of claims 11-20 is industrially applicable.